REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at 858 720 5133.

Status of the Claims

Pending claims

Claims 1 to 27 are pending.

Claims added in the instant amendment

In the present response, new claims 28 to 33 are added. Thus, after entry of the instant amendment, claims 1 to 33 will be pending and under examination.

Allowable subject matter

Applicants thank the Examiner for finding that claims 4, 14 and 16 appear to be allowable over the prior art.

Outstanding Rejections

Claim 19 is rejected under 35 U.S.C. §112, second paragraph. Claims 17, 26 and 27 are rejected under 35 U.S.C. §112, first paragraph, as a "new matter" rejection. Claims 3, 15, 18 to 24, 26 and 27 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention ("written description requirement"). The rejection of claims 1 to 3, 5 to 13 and 15 is maintained and claims 17 to 27 are newly rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention ("enablement requirement"). Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the amended claims. For example, support for specific hybridization conditions to define nucleic acids or polypeptides used in the methods of the invention can be found, inter alia, in the paragraph spanning pages 5 to 6 of the specification. Support for claims directed to methods for hydrolyzing α-glycosidic bonds in saccharides such as raffinose, stachyose, and verbascose, can be found, inter alia, on page 2, second paragraph. Accordingly, no new matter has been added and the amendment can be properly entered.

Objections to the Claims

The Patent Office objected to claims 17, 20 and 21. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, second paragraph

The Patent Office objected to claim 19 for reasons related to antecedent basis. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, first paragraph

New matter

Claims 17, 26 and 27 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement of section 112. This is a "new matter" rejection.

In particular, it is alleged that there is no support in the specification for the hybridization conditions that define the alpha-galactosidase-encoding nucleic acids that hybridize under those conditions to SEQ ID NO:3 in claims 17, 26 and 27. The instant amendment addresses this issue.

Written Description

Claims 3, 15, 18 to 24, 26 and 27 are newly rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the

application was filed had possession of the claimed invention ("written description requirement").

The Patent Office notes that the specification discloses the structure of the alpha-galactosidase of SEQ ID NO:4.

However, the Patent Office alleges that because the specification is silent with regard to which fragments of the exemplary enzyme have function, because the specification does not define structural features necessary for activity for the genus of polypeptides having alpha-galactosidase activity used in the claimed methods, and because only a single species of the genus is disclosed, one skilled in the art could not have reasonably concluded that the inventors at the time the application was filed had possession of the claimed invention.

Applicants respectfully submit that the claimed invention is sufficiently described in the specification so that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing. Applicants respectfully submit that describing a genus of polynucleotides in terms of physico-chemical properties (e.g., a % sequence identity or stringent hybridization to an exemplary nucleic acid, e.g., SEQ ID NO:4) and function (e.g., encoding a polypeptide having alpha-galactosidase activity) satisfies the written description requirement of section 112, first paragraph.

Applicants respectfully aver that the disclosed alpha-galactosidase species of the invention, SEQ ID NO:4, is sufficient to put one of skill in the art in possession of the attributes and features of all species within the genus used in the claimed methods. In fact, both the Patent Office and the Federal Circuit set forth conditions where a single species is sufficient to put one of skill in the art in possession of the attributes and features of all species within a genus, where the genus is defined in terms of shared physical and structural properties with the single species.

Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph, and note that the guidelines state that a description of a genus of polynucleotides in terms of its physico-chemical properties, e.g., a % sequence identity, to a single exemplary species, and a common function satisfies the written description requirement of section 112, first paragraph, for the genus of polynucleotides.

In Example 14 of the Guidelines (a copy of which is attached as Exhibit A), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of Example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogously, the genus of nucleic acids used in the methods of the invention is described by structure (the exemplary SEQ ID NO:4), a physico-chemical property (a percent sequence identity to an exemplary sequence or stringent hybridization to a nucleic acid encoding SEQ ID NO:4) and function (having alpha-galactosidase activity). All species of the genus used in the claimed methods (after entry of the instant amendment) must have at least 70% or more sequence identity to a sequence as set forth in SEQ ID NO:4. Because the USPTO guidelines recognize that written description is met for a genus of polypeptides described by structure, a physico-chemical property (e.g., a % sequence identity) and a defined function, the genus of polypeptides used in the claimed methods also meet the written description requirements of section 112.

The genus of polypeptides used in the claimed methods also fully complies with the requirements for written description of a genus as set forth, inter alia, in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997). In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) Lilly, 43USPQ2d at 1406.

As noted above, the instant claims clearly set forth specific structural and physical characteristics of the alpha-galactosidases used in the claimed methods. In one aspect, the genus of polypeptides used in the claimed methods all must have alpha-galactosidase activity and a specific physical characteristic, e.g., a % sequence identity to the exemplary SEQ ID NO:4. Therefore, the genus of alpha-galactosidases used in the claimed methods is defined via shared physical and structural properties in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

> More recently, the Federal Circuit stated
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> Similarly, in this court's most recent pronouncement, it noted:
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> > More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.
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> Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the function of the alpha-galactosidases used in the claimed methods is sufficiently correlated to a particular, known structure (the exemplary sequence) and a physical (physico-chemical) property (percent sequence identity or stringent hybridization). Accordingly, the species of polypeptides used in the claimed methods are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Regarding the Patent Office's concerns that the specification does not define structural features necessary for activity for the genus of polypeptides having alpha-galactosidase activity used in the claimed methods, Applicants' respectfully aver that it was not necessary for the specification to describe such structural features to convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in

possession of the claimed invention. As discussed above, because the alpha-galactosidases used in the claimed methods were sufficiently correlated to a particular, known structure, physical (physico-chemical) property and function, the species of polypeptides used in the claimed methods were described in terms that conveyed with reasonable clarity to those skilled in the art that Applicants at the time of the invention were in possession of the claimed invention.

Furthermore, in the USPTO written description guidelines (Example 14) a protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B were found to meet the written description requirements without setting forth any specific structural features.

Example 14 of the USPTO written description guidelines notes that procedures for making proteins with substitutions, deletions, insertions, and additions were routine in the art and an assay was described which identified other proteins having the claimed catalytic activity.

Similarly, as stated in the attached expert declaration by Dr. Jay Short, who was an expert in the field of molecular biology and enzyme development at the time of the invention, procedures for making alpha galactosidase fragments and sequence variations, e.g., with substitutions, deletions, insertions, and additions, were routine in the art at the time of the invention. Dr. Short declares that procedures for identifying alpha galactosidase fragments and variants were conventional and routine in the art at the time of the invention. Dr. Short declares that procedures for identifying polypeptides having alpha galactosidase activity were conventional and routine in the art at the time of the invention. For example, an assay for identifying polypeptide having alpha galactosidase activity described in the specification in Example 2, on pages 18 to 19.

Dr. Short declares that one of ordinary skill in the art using the teaching of the specification could have made and expressed nucleic acids encoding alpha galactosidases having a percent sequence identity to the exemplary SEQ ID NO:4, or, which hybridized under defined conditions to the exemplary SEQ ID NO:4, and using routine screening could have determined with predicable positive results which of those nucleic acids encoded a polypeptide having alpha galactosidase activity. Dr. Short declares that using the teaching of the specification one of ordinary skill in the art would have been able to ascertain the scope of the genus of alpha

galactosidases used in the claimed methods with reasonable clarity and recognized that Applicants' were in possession of the claimed invention at the time of filing.

Accordingly, in light of the above remarks, Applicants respectfully submit that the pending claims meet the written description requirements under 35 U.S.C. §112, first paragraph.

Enablement

The rejection of claims 1 to 3, 5 to 13 and 15 is maintained and claims 17 to 27 are newly rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention ("enablement requirement").

The Patent Office states that the specification is enabling for a method for hydrolyzing α-glycosidic bonds by using the α-galactosidase of SEQ ID NO:4 (please see section 11 of the office action).

However, it is alleged that the specification does not provide reasonable enablement for a method of hydrolyzing α-glycosidic bonds using the genus of α-galactosidases as claimed. In particular, the Patent Office remains concerned that because the claimed genera is very large and there is no disclosure of structural elements which correlate with α-galactosidase activity, one of skill in the art might have to go through the burden of undue experimentation to make the genus of polypeptides used in the claimed methods.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of alpha galactosidases to practice the claimed invention. To address the Patent Office's concerns, Dr. Jay Short further declares (see attached and previously submitted Rule 132 declaration) that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art for screening enzymes for alpha galactosidase activity was very high. Dr. Short declares that it would not have been necessary for the skilled artisan to understand which regions of the α-galactosidases used in the claimed methods could be modified to gain a function or activity, or, modified without loss of a function or activity. Dr. Short declares that it would not have been necessary for the skilled artisan to understand which specific regions of α-galactosidase sequence

or structure needed to be modified without affecting function or activity to routinely generate the genus of polypeptides used in the claimed methods. Dr. Short declares that methods for making and screening sequence modifications and enzyme fragments were sufficiently comprehensive, routine and predictable at the time of the invention to predictably generate α-galactosidase-encoding sequences without need of knowing which specific regions of a sequence or structure affected function or activity. Dr. Short declares that methods known at the time of the invention for modifying nucleic acid and polypeptide sequences in combination with high through-put enzyme (α-galactosidase) screening known at the time of the invention, made methods that require previous knowledge of protein structure, including secondary or tertiary structure, active site sequences, and the like obsolete and unnecessary. Dr. Short declares that at the time of the invention, high through-put *in vivo* (e.g., whole cell) nucleic acid expression and enzyme (α-galactosidase) screening protocols were well known in the art. Dr. Short declares that the specification sets forth an exemplary α-galactosidase screening assay to determine if a polypeptide is within the scope of the genus used in the claimed methods (see, e.g., Example 2, of the specification). Dr. Short declares that using methods known in the art at the time of the invention it would not have been necessary to understand which specific regions of α-galactosidase structure needed to be modified to generate a genus of nucleic acids or polypeptides for practicing the invention without undue experimentation. Dr. Short declares that the specification presented to the skilled artisan a rational and predictable scheme for making the genus of α-galactosidases and α-galactosidase-encoding sequences, including a rational and predictable scheme for modifying the exemplary SEQ ID NO:4 with an expectation of obtaining a desired (e.g., new or modified or the same) function. Dr. Short declares that the specification provided sufficient guidance to one of ordinary skill in the art to make and use the genus of polypeptides to practice the methods of the invention.

Accordingly, Applicants respectfully submit that the pending claims meet the written description and enablement requirements under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

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CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first paragraph, and the provisional rejections under the judicially created doctrine of obviousness-type double patenting. Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952. Please credit any overpayment to this account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at 858 720 5133.

Respectfully submitted,

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